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MTI Top 100: Leading Medtechs See Steady Organic Growth In A Market On The Cusp Of Change

ASHLEY YEO ashley.yeo@informa.com

The Top 100 publicly listed and reportable medical technology companies had global sales spanning from more than $30bn to some $100m in the lower reaches, according to the most recent year of fully reported results. As *Medtech Insight*'s sales ranking for the 2018/2018-'19 financial year shows, many of the major changes in value sales were linked to company restructurings. But there were some impressive organic gains, too.

It would be surprising – not to say disquieting – if, in mature industry sectors, the complexion and composition of the leading companies changed radically year to year.

For medtech, a truly unique industry in terms of both the risk assumed by companies and what the ultimate customer – the patient – needs, that would be a pause-for-breath moment. But then, factor in that the medtech industry is itself on the cusp of major disruptive forces, and changes are sure to come as the next decade unfolds.

The consensus is that the industry is readying for the full effects of the digital revolution and potentially new tech industry players; population-based health management, based on big-data analytics and patient engagement; alternative methods of paying for innovation based on outcomes; factoring in harder, perhaps much longer, regulatory processes during a product's premarket journey to commercialization; the market's ongoing shift toward outpatient and remote home care; and the need to continually address the explosion of chronic conditions.

Routinely, the US leads the way in much of the significant change that the global medtech environment eventually comes to embrace; for instance, tackling value-based health care as a long-term need and restructuring health-care buying and delivery structures to prepare for changing demand patterns. The creation of group purchasing organizations as a response to the ongoing consolidation of the US health-care industry, and integrated delivery networks that aggregate buying power for hospital groups, are clear examples.

CLICK

Visit https://bit.ly/2PbPhmY to see the Top 100 and Top 10 segment tables.

Developments that disrupt the norm put pressure on medtech selling prices and require changed behavior at company level. And add to that the fears that the temporarily repealed 2.3% US medical device tax may restart on 1 January 2020, and it is plain that companies in this market must tread ever carefully to maintain a competitive advantage. Good managers may well trade on uncertainty and thrive on unpredictability, but uncertainty for medtechs is everywhere right now, from the EU Medical Device Regulation (MDR), to Brexit, to the US/China trade standoff, to wholesale medtech restructuring.

A VACANCY AT MEDTECH RANKING NO. 25

However, in 2018, with isolated episodes of major M&A, the medtech top rankings stayed largely – and reassuringly – the same. Absent the acquisition of CR Bard Inc. by Becton Dickinson in the closing days of 2017, and the 2018 table lists the same names in the leading 25 companies as in 2017. Robotics pioneer Intuitive Surgical Inc.; Thermo Fisher Scientific Inc., the sixth-largest global IVD player; and Edwards Lifesciences Corp., the heart valve and critical-care monitoring specialist, are vying for the vacant slot created by Bard. They all recorded impressive gains in 2018 to reach the level of $3.7bn sales.

None of those firms used externally added muscle in putting on sales growth of 18.6%, 6.8%, and 8.4%, respectively. They are all at, or ahead, of the average mid- to high-single digit-growth of the global market in 2018, which was worth an estimated $425bn ($397bn in 2017), according to Fortune Business Insights.

Fifteen US groups are among the leading 25 medtechs globally, with three from Japan and seven from Europe – the Netherlands, Switzerland, Spain, the UK and Germany (3). Their activities span the range of device-therapy areas, as shown in our major industry

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Corindus envisions robot network
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The physician who led the first-in-human robotic-assisted neurovascular intervention with Corindus' CorPath GRX system believes the technology could revolutionize neurovascular intervention by allowing a centralized interventional team to remotely treat patients.

Device Week: Oh no, EtO!
https://bit.ly/36uqJez

Over the past year, a number of medical device sterilization facilities that use ethylene oxide, or EtO, have shut down as state regulators have raised concerns about their potential environmental impact. On this episode of our weekly podcast, we discuss what's happened to date, as well as where this EtO issue is headed in the future.

Patent problems for Edwards
https://bit.ly/2E5TWAn

The US Patent Office has rejected a request by Edwards LifeSciences to review an Abbott patent on heart-valve technology, which could establish the patent as a key part of Abbott Laboratories' arguments in a larger ongoing intellectual property case.

Execs On The Move
https://bit.ly/2t6hvH7

Owens & Minor finance boss joins drug-delivery device maker Intersect ENT; operations VP at MicroPort joins bioprosthetic heart maker Carmat; Dynatronics CEO will head neuromodulation product firm BrainsWay in January; and more.

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SHAWN M. SCHMITT @MEDTECHSHAWN
shawn.schmitt@informa.com

REED MILLER @MEDTECHREED
reed.miller@informa.com

AMANDA MAXWELL @MEDTECHAMANDA
amanda.maxwell@informa.com

MARION WEBB @MEDTECHMARION
marion.webb@informa.com

SUE DARCEY @MEDTECH_INSIGHT
sue.darcey@informa.com

FERDOUS AL-FARUQUE @MEDTECH_DANNY
danny.al-faruque@informausa.com

ELIZABETH ORR @ELIZABETHJORR
elizabeth.orr@informa.com

CATHERINE LONGWORTH @MEDTECHCATE
catherine.longworth@informa.com

ASHLEY YEO @ASHLEYPYEO
ashley.yeo@informa.com

MAUREEN KENNY @SCRIPREGMAUREEN
maureen.kenny@informa.com

NEENA BRIZMOHUN @SCRIPREGNEENA
neena.brizmohun@informa.com

VIBHA SHARMA @SCRIPREGVIBHA
vibha.sharma@informa.com

ANDREA CHARLES CUSTOM CONTENT
andrea.charles@informa.com

JANET HANIAK SENIOR DESIGNER

GAYLE REMBOLD FURBERT HEAD OF PUBLICATION DESIGN

RICHARD FAINT HEAD OF MEDTECH
richard.faint@informa.com

PHIL JARVIS MANAGING DIRECTOR

TO SUBSCRIBE, VISIT
medtech.pharmaintelligence.informa.com

TO ADVERTISE, CONTACT
christopher.keeling@informa.com

EDITORIAL OFFICE:
601 Third Avenue, New York, NY 10158 US
phone 212-520-2700

CUSTOMER CARE:
clientservices@pharma.informa.com
US Toll-Free .....+1 888 670 8900
US Toll .....+1 908 547 2200
UK & Europe .....+44 (20) 337 73737
Australia .....+61 2 8705 6907
Japan .....+81 3 6273 4260

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Cybersecurity: Guidance Docs To Come, But Legacy Devices Still A Challenge

ELIZABETH ORR elizabeth.orr@informa.com

Two major documents on medical device cybersecurity will likely be issued in the next several months, a US Food and Drug Administration official said at this week's FDA/CMS Summit in Arlington, VA.

The first document, from the International Medical Device Regulators Forum (IMDRF), offers international consensus guidelines on device cybersecurity. The comment period closed on 2 December, and the IMDRF is aiming to release a final version within six months, said Linda Ricci, a health scientist in the agency's Office of Device Evaluation.

The FDA took the lead in drafting the IMDRF guide, giving the document extra weight as a preview of the agency's thinking. *(Also see "US, Canada Setting Trend For Global Cybersecurity Guidance" - Medtech Insight, 24 Oct, 2019.)*

"The FDA looks to these IMDRF documents and how they are written to help formulate and to help guide our policy," Ricci said. "This is a very good document to look to to see how our policy is likely to move forward and what we're thinking about. So, stay tuned in the spring for the final document."

Meanwhile, the agency is drafting its own guidance document on premarket cybersecurity and is also hoping for a spring release, she said, pointing out that medical device cybersecurity affects all stakeholders.

"Thinking about cybersecurity is not just a medical device manufacturer's responsibility, but everyone in the ecosystem," Ricci said. "Once the device is deployed, what does that mean for what a provider will need to do? What does that mean for what the health system will need to do? If it's deployed to the patient, what is it that they need to do? How are those requirements conveyed to that stakeholder and are they even able to fulfill those types of requirements?"

And the agency's messaging has changed as the public becomes more sophisticated about cybersecurity issues, she said.

For example, the FDA was initially reluctant to publicly disclose known software vulnerabilities before a patch was available because the agency believed it could provide a tempting target for hackers. But at recent patient advisory committee meetings, patients made it clear that they want to know about any potential risks tied to wearable or implanted devices, Ricci said. *(Also see "Let's Talk About Cybersecurity: US FDA Wants Feedback On Safety Alerts" - Medtech Insight, 8 Jul, 2019.)*

"I think all the stakeholders in this area will continue to advance in their knowledge and their ability to discuss it," she said. "And like it or not, we're all stuck with cybersecurity in all of our daily lives. So, I think we will all become more educated about how to protect ourselves, and that will extend to our jobs, our medical devices and our hospitals. Everybody will become more savvy, and as such, our communications will need to reflect that."

LEGACY DEVICES POSE CHALLENGES

The 3 December session at the FDA/CMS Summit also touched on cybersecurity for legacy devices, especially those that run on software based on 2001's Windows XP or 2009's Windows 7 operating systems. Cybersecurity for devices using older versions of Windows has become more urgent since Microsoft announced plans to phase out technical support for them early next year.

The FDA is working with stakeholders on alternate security measures that can help compensate if a device's basic software can't be updated, Ricci said. Further, the agency's most recent guidance document on device modifications specifically allows manufacturers to skip notifying the FDA about upgrades made purely to increase cybersecurity.

The agency is also trying to spread awareness about device software updates and their patient safety benefits to healthcare providers.

"We're making sure that every player in the ecosystem understands their responsibility and helps to make the legacy devices safe and secure for patients," Ricci said. "And then, looking forward, making sure we're not creating additional legacy devices that somebody else is going to have to deal with."

PHYSICIAN GROUP SEEKS MORE CLARITY

Paul Westfall, Washington counsel for the American Medical Association (AMA), echoed Ricci's concerns about legacy device cybersecurity. He added that physicians are often flummoxed by what they see as a lack of transparency from manufacturers about costs related to software patches and updates. That knowledge should be offered upfront to allow providers to make more educated purchasing decisions, he said.

Westfall also recommended that manufacturers center the patient-physician relationship in discussing cybersecurity issues, because those concerns tend to resonate with physicians.

Physicians are more willing to adapt new software or other technology if it works well, integrates easily into their workflow, and the physician gets paid for the time spent using it, he said. For example, some device-related software amounts to "an Excel spreadsheet with a bunch of Scotch tape," and requires doctors to put in extra time and effort to duplicate information already in the electronic health record (EHR).

"What we're really looking for are the situations where you have one solution for 10 problems, and not 10 solutions for one problem," Westfall said.

AMA LOBBIES FOR STARK LAW CHANGES

Westfall also addressed the AMA's reaction to pending changes to the Stark anti-kickback law that will create new "safe harbors," allowing particular types of gifts to physicians. Certain types of technology, like traffic-monitoring software and security-risk assessments, would be protected. *(Also see "HHS Plans New Anti-Kickback Statute 'Safe Harbors,' Stark Law Changes, To Promote Value-Based Care" - Medtech Insight, 10 Oct, 2019.)*

The group is basically happy with the proposal, but says computer hardware donations should also be included in the safe harbors. The US government has argued that these donations could too easily be used to protect gifts of hardware that can be put to multiple uses, such as network servers.

Westfall said the AMA is recommending two potential solutions:

- The rule should be changed to allow hardware donations when the hardware is used only to operate a permitted software donation; and
- The anti-kickback law should allow hardware donations when they're made as a reward for a cybersecurity threat assessment performed by the donor.

"We see a lot of sticks, but we don't see a lot of carrots or positive incentives," Westfall said. "So, we see that as a very, very, very good positive incentive that if you did the cybersecurity risk assessment time, that will allow you to receive hardware for cybersecurity expenses."

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MDR/IVDR Corrigenda Due Final Sign-Off Soon; Big Changes For Devices, Less So For IVDs

AMANDA MAXWELL amanda.maxwell@informa.com

European Parliament

The final adoption of measures to increase the number of medical devices eligible for an additional four years on the market, beyond the 26 May 2020 full application of the EU Medical Device Regulation (MDR), is imminent. The measures benefit medical devices that are already CE-marked as class I under the Medical Devices Directive (MDD), but which are being upclassified under the MDR.

A spokesperson for the European Parliament told *Medtech Insight* that the vote on the latest corrigenda to both the MDR and IVD Regulation (IVDR) was due to take place at the European Parliament's plenary session on 16-19 December.

ENVI VOTE ON 3 DECEMBER

This tabling of the plenary vote follows fast on the heels of changes to both regulations by the European Parliament's committee on the environment, public health and food safety (ENVI), on 3 December 2019.

The vote should be no more than a formality, although one MEP, while recognizing the urgency of adopting the cor-

rigenda, questioned an anomaly that had occurred in this case. Speaking to the ENVI committee on 3 December, Biljana Borzan, a Socialists and Democrats MEP from Croatia, noted that the MDR corrigendum was being used to make changes to the substance of the regulation, rather than simply to correct technicalities and inconsistencies, as is the role of a corrigendum.

NO MORE IVDS ELIGIBLE FOR GRACE PERIOD

Attention has focused on the news surrounding class I upclassified products under the MDR, but there is no such equivalent change under the corrigendum to the IVDR.

Given that the some 85%-90% of IVDs will need to involve a notified body for the first time under the IVDR, compared to the 10%-15% that need to involve one now under the IVD Directive, the diagnostics industry has been hoping that there would be a concession for more IVDs to benefit from a two-year grace period (between 26 May 2022, when the IVDR full applies, and 26 May 2024).

At present, the only products that can potentially benefit from this grace period are the 10%-15% of IVDs that require notified body involvement, ie, products that fall into List A or B of Annex II under the IVD Directive, as long as there are no significant changes in their design or intended purpose.

But there is nothing in the IVD corrigendum to suggest this, and it is not known whether there might be another corrigendum to the IVDR that could contain such a measure.

Instead, the bulk of the amendments are related to the Eudamed medical device database and reflect those that are also contained in the MDR corrigendum. The language used is also equally difficult to understand.

ONE IVD RISK-CLASS CLARIFICATION

The only significant change impacting IVDs specifically is that devices intended to be used in determining feto-maternal blood group incompatibility are now included in classification rule 2 in Annex VIII, section 2.2.

This means they are considered class C (the second-highest risk class), except when intended to determine any of the following markers: systems for blood-group typing; Rhesus; Kell; Kidd; and Duffy. In those cases, they are classified as class D (the highest risk class).

GOOD NEWS FOR THE MEDICAL DEVICE SECTOR

Granting an extra four years to medical devices currently regulated as class I under the MDD, and moving them into a higher class under the MDR, is very good news for the medtech industry. It will not only take the pressure off manufacturers of those products that will benefit from an additional four years to comply, but it may also relieve the extent of bottlenecks that are being predicted at notified bodies in the run-up to the 26 May full implementation date of the new regulations.

This should give notified bodies more time to focus on those products that have no choice but to comply by the 26 May deadline. But the medtech industry remains seriously held back by the slow and piecemeal implementation of the new regulatory framework. In addition, some may question whether this extra time might push bottlenecks further down the line, so that most medical devices are being evaluated by notified bodies under the MDR at the same time as there is a swell in numbers of IVD companies attempting to get conformity assessment for their products from notified bodies – most for the first time.

SO WHICH MEDICAL DEVICES STILL NEED TO COMPLY BY 26 MAY?

Medical devices that will need to comply by the 26 May deadline are:

- All class I products that are not being upclassified (although the majority do not need the involvement of a notified body);
- Products that fall under the MDR for the first time, such as Annex XVI products that do not have an intended medical purpose; and
- Products in classes IIa, IIb and III, which undergo "significant changes in the design and intended purpose."

PREVIOUS CORRIGENDUM TO MDR AND IVDR

This is the second set of corrigenda to the new regulations. The main changes in the first set of corrigenda to the MDR and IVDR were as follows:

MDR

- Products of animal origin that had been legally placed on the EU market before 26 May 2020 will not be allowed on the market after that date in those member states that previously allowed them; and
- Accessories to Annex XVI devices – those without a medical purpose and mainly used for asthetic purposes – will no longer be classified in their own right under the MDR, but are instead classified as part of the product itself.

IVDR

- The surveillance assessment will include the surveillance of technical documentation for class B and C devices by the notified body. The aim of surveillance is to ensure that the manufacturer fulfils the obligations arising from the approved quality management system.

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Tech Companies Grappling With A Brave New World Of Regulations While Developing Digital-Health Products

FERDOUS AL-FARUQUE danny.al-faruque@informa.com

While there's been an exponential growth of tech companies entering the medical device arena – and digital health in particular – these traditional firms have begun heavily investing to better understand an unfamiliar US medtech regulatory system, industry experts say.

Bakul Patel, associate director for digital health at the Food and Drug Administration's Center for Devices and Radiological Health (CDRH), said he's seeing a lot of tech companies not traditionally in the medical device space trying to figure out how the FDA's regulations affect their product development. During a panel session on 4 December at the FDA/CMS Summit in Arlington, VA, Patel told *Medtech Insight* that companies are reaching out to the FDA long before their product is ready for review to get answers, using channels such as the agency's pre-submission process.

"I definitely see a lot of entrepreneurs who are exploring this space asking us way ahead of time: I have read some of these guidances, I want to do the right thing, what do I need to do?" – Bakul Patel

As the FDA considers how it will approach digital-health product regulation, it has put out a number of guidance documents that tackle commodities such as wellness products and health apps, which can give companies better insight into the agency's thinking. The FDA says it will use regulatory discretion to not enforce regulation of low-risk digital-health products.

"I definitely see a lot of entrepreneurs who are exploring this space asking us way ahead of time: 'I have read some of these guidances, I want to do the right thing, what do I need to do?'" said Patel, who – as the top FDA official overseeing digital health – coined the term "software as a medical device" (SaMD) and is developing the agency's pre-certification program that would allow SaMDs on the market based on how much the FDA trusts a company's corporate culture.

He said the agency has seen an uptick in the number of questions coming from traditional software companies, noting that the FDA's digital health inquiry inbox used to get on average an email a day – but now there are two or three.

Since the FDA began working with the International Medical Device Regulators Forum to develop best practices to oversee digital-health products, more and more tech companies have emerged to get clarity on how their digital-health products may be regulated, Patel said. He added that the quality of questions has also elevated, which has shifted the agency's own thinking on the topic.

HIRING REGULATORS

And over the past few years, major tech companies entering the medical device arena have also bolstered their ranks by hiring former FDA regulators.

When Apple Inc. successfully received de novo authorizations for health apps on its latest watch, the company hired – among others – Donna-Bea Tillman, a former CDRH reviewer with 17 years of experience, to file the company's premarket application to ensure they didn't face regulatory roadblocks.

Similarly, after former FDA commissioner Robert Califf stepped down from leading the agency in 2017, he was picked up by Google's health spin-off Verily Life Sciences LLC. According to Szymon Perkowski, a software quality manager at Verily, the

company is currently hiring more officials with medtech regulatory experience.

While not all digital-health products are necessarily going to be regulated by the FDA, Perkowski said his software development team still treats all of Verily's digital-health products as if they were already categorized as medical devices.

> "We talk to hundreds of [digital-health] companies a week. The hottest market segment is SaMDs."
> – Jon Speer

Jon Speer, founder of medtech consulting firm Greenlight Guru, echoed Perkowski's sentiments and said it's become common in the digital-health space to ask regulatory questions during development, such as whether the product complies with the FDA's good manufacturing practice regulations.

"I think that's good because I think that [when developing] any software … that should be the premise," he told *Medtech Insight*.

Speer said understanding the FDA's regulatory regime is one of the biggest challenges traditional tech companies are facing as they attempt to enter the medical device space. He added that digital-health developers are realizing that "the world has changed," and medical devices are ubiquitous – whether they are wearable technologies or software on hospital equipment. That means there is a lot of potential for them.

"We talk to hundreds of [digital-health] companies a week," Speer said. "The hottest market segment is SaMDs."

The big question that digital-health companies are now asking, he says, is whether traditional medical device companies were expected to use the same level of "rigor and discipline" that is being expected of them.

'KEY BATTLEGROUND'

Meanwhile, Verily's Perkowski said the relationship between digital-health companies and regulators has also changed. Whereas once interactions were limited to being between the quality management staff inside the company and the FDA, they now include everyone on the development teams. He commended the agency for communicating with these newcomers in a way that has greased the regulatory wheels.

"There is a number of companies trying to transition into medical devices from wellness products," Perkowski said. "The pre-cert program is not your traditional GMP, but is in language any company can understand."

And while he says the pre-cert program is a wonderful vehicle for digital-health regulations, consultant Speer noted that the FDA has already put out a "flurry of good guidances" that help digital-health companies in terms of developing wellness products, mobile-health apps and artificial intelligence/machine learning products.

Speer agreed with Perkowski, noting that medical device regulations that were set in place by the FDA in the 1990s are evolving with the emergence of digital-health products and their iterative nature.

"We have to change the perception of what regulation is and isn't," Speer said. The pre-cert program "is a key battleground for that."

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Performance Criteria Issued On Magnetic Resonance Coils In New FDA Draft Guidance

ELIZABETH ORR elizabeth.orr@informa.com

A new draft guidance from the US Food and Drug Administration sets performance criteria for magnetic resonance (MR) coils, making the devices eligible for the standards-based Safety and Performance Based Pathway.

The pathway allows specific device types that the FDA believes have an established safety profile to be cleared based on compliance with guidance documents, consensus standards and special controls, eliminating the need for comparisons to a specific predicate device. It is an expansion of the abbreviated 510(k) pathway and was detailed in a final guidance document in September. *(Also see "It's Raining Guidance Docs: FDA Expands Abbreviated 510(k) Program" - Medtech Insight, 23 Sep, 2019.)*

"If your device is appropriate for submission through the Safety and Performance Based Pathway, and you choose to use

that option, you do not need to provide direct comparison testing against a legally marketed predicate device to demonstrate substantially equivalent performance characteristics," the FDA's draft document explains. Instead, the agency recommends manufacturers submit a results summary for all tests evaluated and specific submission information, such as declarations of conformity, for each test or evaluation.

Other device types already deemed eligible for the Safety and Performance Based Pathway include conventional Foley catheters, cutaneous electrodes for recording purposes, spinal plating systems, and orthopedic non-spinal metallic bone screws and washers.

The draft, dated 9 December, applies to class II MR coils used in hydrogen- and proton-imaging devices. The document specifically exempts coils that make more than "minimal" contact with a patient's body, as well as those indicated for specific diagnostic or treatment functions.

Sponsors submitting MR coils via the abbreviated pathway are asked to show compliance with these seven separate performance tests:

- Image signal to noise;
- Image uniformity;
- Surface heating;
- Acquired image quality;
- Decoupling;
- Electromagnetic compatibility; and
- General mechanical and electrical safety.

The FDA's draft document lists multiple international standards documents that can be used to establish the performance standards.

Further, the coils should be evaluated for biocompatibility factors such as irritation and cytotoxicity. But if the new device is identical to its predicate in terms of raw materials, manufacturing processes and type and duration of tissue contact, and any changes in geometry aren't expected to alter the biological response, the FDA will typically consider that to be sufficient evidence to establish substantially equivalent biocompatibility, the draft states.

The document is open for public comment at www.Regulations.gov under docket No. FDA-2019-D-1650 through 28 February 2020.

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A COMPLIANCE 360° Q&A

Analyzing Quality Data Is Essential. Here's What One Expert Says Your Firm Should Do To Stay In FDA's Good Graces

SHAWN M. SCHMITT shawn.schmitt@informa.com

Medical device manufacturers should make sure they have adequate resources to analyze quality data they take in so they can prevent the recurrence of nonconforming products, processes and procedures.

That's just one message about good quality data practices from Ricki Chase, compliance practice director for Lachman Consultant Services and a former US Food and Drug Administration investigations branch director. She says a failure to provide data-analyzing resources in a timely way is "a frequent shortcoming" for firms.

"Consideration should be given to the resources necessary to perform this critical quality function properly," Chase told *Medtech Insight*.

"Capturing data in real time and having systems in place that can quickly identify outliers or trends toward alert or action limits is best practice," she added. "However, manufacturers must have a scientific rationale for setting such alert or action limits, and a use of data-generating, automated, manufacturing processes is a good way to capture quality data in a timely fashion."

And Chase reminds companies that software used to store, track, and analyze quality data should be validated.

"A lack of validation calls into question the integrity of your data sources and the decisions stemming from it," she said. "As part of the validation, you must ensure the security of the data from inappropriate deletion, write-over or manipulation."

Medtech Insight: OK, let's start with the basics when it comes to collecting quality data. What does the US Food and Drug Administration say about it?

Ricki Chase: Well, the FDA specifically calls out in its Quality System Regulation [in Sec. 820.100(a)(1), "Corrective and Preventive Action,"] a requirement to, quote, "analyze processes, work operations, concessions, quality audit reports, quality records, service records, complaints, return products, and other sources of quality data with the intent to identify existing and potential causes of nonconforming product, or other quality problems."

It is important, firstly, to understand that the, quote, "other sources of quality data," are those which the manufacturer would most likely be aware of and be reasonably expected to use when assessing for nonconformances or other quality matters. The burden is placed on the firm to demonstrate why a quality factor is not being assessed. So, the best way to meet the spirit of the regulation and to promote the safety and efficacy of your device is to identify the quality factors that are meaningful to your sus-

tainability. A step-by-step analysis of the design and the manufacturing processes should be performed to determine the sources of data available for your evaluation. It is not enough to simply examine those data sources specifically noted in the regulation.

For example, many people do not consider rejected products stemming from a manufacturing process or an inspection process to be considered a quality datapoint. Instead, it is seen as a profitability loss, when in fact, if a product is rejected, it should be understood what caused the product not to meet standards and the effect of that cause on consistent manufacture of the device needing specification, or the design of the device.

What should a device maker do after it identifies its sources of quality data?

Chase: Once you have defined the quality data you will monitor, you should commit to procedure certain factors, such as the source of the data, how frequently you will capture the data, frequency of analysis, and how the data will be used in decision-making, when the data will be acted on if a nonconformance or a potential quality issue is identified or suspected, and how reactions to quality indicators will be documented to demonstrate your response to the quality indication.

Does the FDA expect companies to trend their data?

Chase: The Quality System Regulation does not use the term "trend." Nowhere does the regulation require you trend quality data. And this is frequently pointed out when the FDA has conducted an inspection where data-trending is not occurring.

However, a review of the preamble to the regulation makes the FDA's opinion very clear: You must use statistical techniques to analyze your data. Those statistical techniques should be identified in a procedure and shall be appropriate for the analysis being performed. If you choose not to trend your data, then you should be able to explain how you are capturing and analyzing the data to determine if nonconformances or potential quality problems exist. The FDA has long been aware of company attempts to dilute data or manipulate statistical techniques to reduce the appearance of quality problems.

What's a common mistake that firms make when it comes to quality data?

Chase: A common practice is to state in a procedure that complaints will be monitored on a per-volume basis, and that a corrective action will only be taken if the complaints for a particular failure mode exceed X percent of the volume.

But when the manufacturer makes millions of devices annually, it is not a reasonable position to make a blanket statement that action will only be considered if the complaints exceed, say, 1% of the devices manufactured. This demonstrates a lack of understanding of the value and intent of the Quality System Regulation. Further, regardless of volume of devices manufactured, any failure of a device leading to death or serious injury requires an investigation into potential quality failures. A frequently overlooked area of quality data lies within the design process. The risk assessment performed during the design should identify potential failure modes and the risks associated with each. For high-risk failures, it's expected that you will have methods in place to capture and analyze quality data to verify that these failure modes are not occurring. There are very large amounts of quality data available to the manufacturer from both internal and external sources.

And what are the FDA's expectations when it comes to postmarket data?

Chase: Postmarket data is of extreme interest for the FDA. More and more it is expected that a robust system of monitoring your device in the marketplace will be employed to detect potential problems or risks. There is little room to state that you did not know or did not understand the expectation, which has been widely communicated by the agency. The focus is on using postmarket signals to create a proacting and predictive method of using data to improve your overall quality system.

And the FDA is also very interested in the patient experience. If data exists indicating that patient interaction or physician interaction with the device is problematic or prevents use because it is too complicated, that is information you are expected to understand and address regardless of it presenting a compliance concern. Given the amount of external sources available to monitor the market of your device – as well as similar devices – you may consider outsourcing the capture of these datapoints.

For example, there are companies that will gather FDA-483 [inspectional observation report] regulatory action, recall and import alert information, and provide that information for your review and consideration. Failing to capture, analyze and respond to quality indicators is a major failure of the corrective and preventative action system. What is worse is having the data and not responding to it, or having little or no justification for the reaction to what the data tell you. You could avoid these pitfalls by developing robust and well-defined procedures, and then following them.

How can, say, a quality or regulatory assurance unit in a device firm best relay to higher-ups that good analysis of quality data is critical?

Chase: Well, if the regulatory and FDA expectations alone do not convince your leadership that quality data are critical to the success and safety of your device, then perhaps money will. Studies have found that adopting quality practices – such as those used by the top-quality performers in industry – can reduce your manufacturing costs by 20% to 30%, and your profits may increase by as much as 3% to 4%.

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RSNA 2019: AI, Machine Learning Continue To Dominate Developments In Radiology

PHIL GREENFIELD phil.greenfield@informa.com

RSNA exhibition showcases AI tech

SIEMENS RAMPS UP AI-BASED RADIOLOGY ASSISTANT RANGE

At last year's RSNA, Siemens Healthineers AG debuted its first AI-based software assistant for radiology, the AI-Rad Companion Chest CT, which automates enhanced visualization of CT images of the lungs, heart and aorta. This year, the company added two more AI-based software assistants that are designed to free radiologists from the burden of performing routine activities during magnetic resonance imaging (MRI) examinations of the brain and prostate.

AI-Rad Companion Prostate MR for Biopsy Support automatically segments the outer contour of the prostate, which can cut the time needed for this activity down to a few seconds. The radiologist then marks the suspect areas and passes the annotated MRI images to the urologist for fusion with the ultrasound images during the biopsy. Targeted, MRI-supported biopsies can make it easier for the urologist to detect significant prostate carcinomas.

This is significant, particularly in Europe, where the European Association of Urology and the National Institute of Clinical Excellence (NICE), UK, have recently incorporated the primary diagnosis of prostate cancer using MRI and MRI/ultrasound fusion biopsy in their guidelines. Fusion biopsy fuses pre-biopsy multiparametric MRI images of the prostate with ultrasound-guided 3D images in real time, allowing for excellent imaging of the prostate and any abnormal changes that may or may not be cancerous. According to a recent report from Informa's Meddevicetracker, fusion biopsy is expected to see strong market growth over the next five years. *(Also see "Market Intel: Precision Diagnostics And Focal Treatments Offer Personalized Approach To Prostate Cancer" - Medtech Insight, 25 Oct, 2019.)*

AI-Rad Companion Brain MR for Morphometry Analysis automatically segments the brain in MRI images, measures brain volume, and marks volume deviations in result tables used by neurologists for diagnosis and treatment.

Both new apps, which are not yet cleared for sale in the US or CE-marked in Europe, can be used on MRI scanners from different manufacturers, including GE Healthcare and Philips Healthcare, and are available on Siemens' teamplay, a secure cloud-based health-care platform designed to integrate seamlessly into existing clinical workflows. Peter Koerte, head of digital health at Siemens Healthineers, said further applications, for radiography and radio-oncology, would follow. *(Also see "Exec Chat: Deepak Nath, President Of Siemens Healthineers' Laboratory Diagnostics, Offers An Insider's Look At AACC 2019 " - Medtech Insight, 9 Aug, 2019.)*

PHILIPS HEALTHCARE WORKING ON AI WORKFLOW INTEGRATION

Philips Healthcare demoed its in-development IntelliSpace AI workflow suite, which enables health-care providers to integrate AI applications into the imaging workflow. Leiden University Medical Center in the Netherlands recently signed an agreement to be the first health-care provider to install the platform *(Also see "Market Intel: AACC 2019 – Roundup Of The Top 5 Diagnostics Companies" - Medtech Insight, 19 Aug, 2019.)*

The company has several partners that provide applications on the IntelliSpace AI Workflow Suite. These include:

- Aidoc – The Israeli developer of AI-based medical imaging software provides applications for intracranial hemorrhage, C-spine fractures and pulmonary embolism.
- MaxQ AI – Another Israeli company, which supplies the ACCIPIO intracranial hemorrhage (ICH) and stroke platform. ACCIPIO is the company's first medtech platform and uses AI for assessment of non-contrast head CT for ICH diagnosis and treatment.
- Quibim – The Spanish company provides applications including brain lesions detection, chest X-ray classifier, emphysema, liver fat and iron concentration, and brain atrophy analysis. Applications from Quibim are not 510(k)-cleared.
- Riverain Technologies – The Miamisburg, OH-based company provides the ClearRead bone suppression and ClearRead CT cancer detection AI software.
- Zebra Medical Vision Inc. – The Israeli medical imaging analytics company's applications help detect ICH and pneumothorax. In November, Zebra secured 510(k) clearance for HealthCXR, intended for the identification and triaging of pleural effusion in chest X-rays. The company now has four

FDA-cleared products as part of its AI1 bundle of triage and prioritization applications for chest X-rays. *(Also see "Zebra Medical Lands $30m From aMoon, J&J For AI-Driven Imaging Tech" - Medtech Insight, 8 Jun, 2018.)*

CHINESE-MADE SCANNER PERFORMS 0.2S CARDIAC SCAN

Chinese company Neusoft Medical Systems introduced its NeuViz Epoch 512-slice CT scanner, which uses organ-specific AI algorithms to identify the anatomy for precision scanning and reduce image noise by 80%, according to the company. Not yet available in the US, the scanner has a large 16cm detector, which means a cardiac scan can be completed in as little as 0.2 seconds, as the table does not need to be moved during the scan, the company claims. The company was formed in 1998 and sells radiology systems and diagnostic products to more than a hundred countries worldwide, including in the US and Europe.

CORTECH LABS' MACHINE LEARNING TOOL COULD PREDICT EARLY AD

San Diego-based CorTechs Labs Inc. presented findings of a study using machine learning to build a brain age-prediction model that could serve as an early biomarker for Alzheimer's disease. The model measures metabolic and volumetric changes of normal brain structures using automation software to combine positron emission tomography (PET) and MRI measurements to predict brain age. According to the company, results of the study suggest that accelerated brain aging could serve as an early biomarker for Alzheimer's and might help clinicians to identify younger subjects with Alzheimer's and monitor their disease progression rates.

The study used the CorTechs' PETQuant software, a research-specific component of NeuroQuant, the company's FDA 510(k)-cleared, CE-marked software for quantitative analysis of MRI images. The company is planning to gain regulatory clearance for PETQuant as a clinical tool in various countries and has a $1.15m grant from the US National Institutes of Health for work to automate the diagnosis and prediction of Alzheimer's disease using PETQuant.

GE HEALTHCARE'S FOCUS ON PRODUCTIVITY AND COST-SAVINGS IN RADIOLOGY

GE Healthcare launched a raft of intelligent apps and smart devices designed to drive efficiency in radiology departments. These included:

- AIR Recon DL, a deep-learning MRI reconstruction technology application designed to improve signal-to-noise and image sharpness, and enable shorter scan times. The app, for which US clearance is pending, was developed using a neural network trained on tens of thousands of images using GE's Edison AI Platform.
- Critical Care Suite, an FDA-cleared collection of AI algorithms embedded on a mobile X-ray device for triage. The algorithms help reduce the turnaround time it can take for radiologists to review a suspected pneumothorax, says GE. In addition, they can reduce image quality errors and improve efficiency by simultaneously auto-rotating images and analyzing and flagging protocol and field of view errors. GE estimates the auto-rotate AI alone can save a user at a medium to large size hospital "more than 70,000 manual clicks that amount to nearly 20 hours, or three working days a year spent rotating chest images on portable X-ray machines."
- Revolution Maxima, a CT scanner with AI-based auto-positioning technology intended to enable one click, hands-free patient positioning (510(k) pending).
- Embo ASSIST with virtual injection, an app designed to aid complex embolization procedures by allowing interventional radiologists to analyze the vasculature and simulate injections to help determine the best embolization strategy to avoid healthy tissues in the brain or prostate.

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EXEC CHAT

Koa Accel Plans To 'De-Risk' Start-Up Investing

REED MILLER reed.miller@informa.com

Koa Accel hopes to improve the success rate of start-up medical device companies by helping inventors bring their technology to market quickly.

Koa Accel CEO Francis Duhay is the former chief of cardiothoracic surgery and cardiology at Kaiser Permanente. He was also chief medical officer at Edwards Lifesciences and led start-up companies including Aegis Surgical, Atrius, Kino Biosciences, Makani Science and Microdermics. Duhay and Ray Chan, a venture capitalist with K5 Ventures, founded Koa Accel in Irvine, CA, in September 2019 to bring a new approach to medtech investing.

CLICK

This is Part 1 of a two-part Exec Chat. Check out Part 2 at https://bit.ly/2YA6BVM.

Koa Accel plans to "accelerate" one new medical device technology each quarter. So far, it has two portfolio companies: Makani Science, which is developing a wearable sensor that continuously monitors a patient's breathing and pulmonary volumes during medical or dental procedures; and Microdermics, which is developing a platform technology for continuous monitoring of multiple analytes with microsensors as small as a mosquito's proboscis.

In a two-part interview with *Medtech Insight* (see "CLICK" box at left), Duhay explains how his past mistakes and successes inform Koa Accel's approach to medtech

investment and how the company hopes to drive "hyper-acceleration" that can reduce the risk of investing in early-stage medtech companies.

Medtech Insight: How did Koa Accel get started?

Francis Duhay: Prior to forming Koa Accel, I was part of a venture capital firm. Over a period of a year and a half, I sat through about 70 pitches from early-stage medical device companies. One of the major takeaways was that in over 90% of cases, the ideas actually were quite clever. Indeed, there was no shortage of great ideas. Of course, we ultimately couldn't invest in them all, and I picked 14. Fast-forward about three years. Nine of those 14 companies disappeared within two years. Of the remaining five, four are "zombies," if you will – "The Walking Dead."

Today, we're left with one possible success. This represents a 93% failure rate, which lends support to what many experienced investors have lamented – the overwhelming majority of early-stage medical device start-ups will fail. Looking back, I thought I had a distinct advantage, having practiced as a cardiothoracic surgeon at a top-flight university hospital, earned an MBA, and spent nearly 10 years as chief medical officer at a major medical device company. But the reality was that my batting average was no better than anybody else's.

My medical training compelled me to investigate this disastrous outcome further. I studied all the start-up failures in great detail, conducting a postmortem on each one, trying to elucidate potential cause and effect. Since the Great Recession [in 2008], many investors have shied away from early-stage medical device companies, citing the long payback period and high failure rate of over 90%. My analysis found that 70% of these failures were, in fact, due to poor business execution or dysfunctional management, or both – not bad technology.

The negative repercussion is that many investors today avoid early-stage medical device companies altogether.

"Many investors have shied away from early-stage medical device companies, citing the long payback period and high failure rate of over 90%. [But] 70% of these failures were, in fact, due to poor business execution or dysfunctional management, or both – not bad technology."
– Francis Duhay

You might say, "Can't medical device accelerators help with that?" I've not seen a good study, but I'm dubious. Indeed, most accelerators generally provide office space, free Wi-Fi, a mentor or two, who advise and perhaps make important introductions for the entrepreneurs but aren't themselves doing the heavy lifting. Indeed, these mentors often are only volunteers, or are spread too thin.

Is this "failure rate" particularly high in medical device companies or is this typical of all start-up investing?

Duhay: A few years ago, I was involved in a biotech company, where I learned that the failure rate was even higher than in medical devices – as high as 99%. So, it could be worse. On the other hand, tackling something with a high failure rate gives you a greater opportunity to make a difference.

Consequently, at Koa Accel, our primary hypothesis is that, if we can obsessively manage risk and convert a 90% failure rate to, say, 60% – which is still not great – that could drive tremendous value in terms of a higher success rate in bringing medical devices to market, and ultimately, a higher return on invested capital for our shareholders.

What kind of relationship are you seeking in the technologies you invest in?

Duhay: That begs the questions: Why do we do what we do? Why does anyone get involved in medical devices? The endgame, of course, is to enhance the lives of all people through the benefits that medical devices confer. At Koa Accel, our mantra is to develop medical devices faster, at lower cost, and with a greater likelihood of a successful exit, while preserving equity ownership for all our shareholders. First, the inventor/founder must acknowledge the complexity of medical device development. That is, they appreciate the need for exceptional business expertise. Surprisingly, many do not – often because they are highly accomplished scientists or physicians afflicted with the "smartest-person-in-the-room" syndrome.

The foundation of Koa Accel is a community of medical device experts whom

we call "value creation providers," or VCPs. Our team of VCPs each bring 10 to 30 years of experience across a dozen areas of business functional expertise, such as IP and corporate law, upstream marketing, product design, regulatory and clinical affairs, medical/scientific affairs, health economics and reimbursement, quality assurance, operations, finance, and, of course, commercialization. They do not act simply as advisors or coaches; they roll up their sleeves and do the heavy lifting, because remember, at this point, there is no team to coach.

To be able to recruit this caliber of VCP into Koa Accel, I recognized the importance of creating a business structure that was a "win-win-win" – not only for the inventor and investors – but also for the VCPs themselves. A major challenge you confront when engaging VCPs, who frequently are busy consultants, is how best to gain mindshare.

We implemented three methods to drive alignment: First, most of our VCPs are former coworkers or are referred by someone I trust, so I started with confidence in their work product. Second, VCPs are compensated with a blend of cash and equity, which is earned by achieving value-based, objective, time-sensitive deliverables. Finally, 90% of VCPs are also investors in Koa Accel.

We drive fast execution, or what I like to call "hyper-acceleration." The major value inflection points for most Koa Accel projects are manufacturing readiness and [US Food and Drug Administration] 510(k) clearance, and we strive to accomplish both within 15 to 18 months. To do this, we leverage the experience, professionalism and competitive nature of our VCPs. Moreover, Koa Accel is incredibly selective about the kinds of technologies we pursue.

We can afford to be highly selective because, again, there is no shortage of great medical device ideas. As a byproduct of hyper-acceleration, we accomplish our objectives at extremely low cost, thereby preserving the equity ownership of all our investors. Our early experience has demonstrated that we can get to manufacturing readiness and 510(k) clearance with less than $500,000 in seed funding. This is extremely challenging and is driven by Koa Accel's culture of fiscal discipline. VCPs are also owners who reap tremendous benefits by skipping a financing round.

Can you describe Koa Accel's operations when working with a new company?

Duhay: As I mentioned, medical device development is extremely complicated. When I whiteboard the process I describe at least a dozen "buckets" of competencies. Importantly, the first bucket is entitled "research," which is often conducted in a university or hospital setting. Because most medical device start-up ideas come from scientists and physicians, many early-stage medical device companies are run by "researchers."

The obvious problem is that these novice entrepreneurs are mainly familiar with the first bucket. To improve the odds of success, some scientists and physicians might consider assembling a team of business functional experts on their own. Yet, most lack the professional networks, shrewdness – eg, discriminating between a reputable regulatory consultant from a poseur, and financial capital to do so. Let's face it, good business consultants are expensive.

At Koa Accel, we have a large network of experienced VCPs, anywhere from three to five experts in each bucket. Each has between 10 and 30 years of experience in the medical device industry. Depending on the specific needs of the medical device project, a team could comprise between five and 10 individuals, who are handpicked by experience, skill and desire.

I first conceived of the Koa Accel process as an academic exercise, thinking that it might make an interesting business article or blog. I informally met with about 70 colleagues within my professional network, most of whom fit the profile of a VCP today. During these interviews, two patterns emerged. First, they grasped the concept instantly – they all had worked for, or consulted with, medical device start-ups or established companies with great technology – only to watch management fumble and destroy value time and time again.

Among those who were active consultants, not even one had ever profited from a big exit – and they were incredibly frustrated. And second, they all wanted in. The other imperative of Koa Accel, in addition to optimizing business competencies, is optimizing resources. Most seasoned investors have experienced situations where technology left the university lab too early. In other words, it still needed additional work to advance it to the product-development stage.

To prevent this, rather than replicate a university lab outside the university's walls, Koa Accel invests time to educate prospective inventors on specific marketing requirements we derive from exploratory market research, which involves gathering prospective customer feedback. With this information in hand, we sit down with the scientist to discuss how close she thinks she is to achieving these requirements.

This conversation is frequently a revelation for the scientist. Sometimes, they report that the requirements are already achieved, or achievable within six months. In this case, our due diligence advances to the next level. Other times, they confess being at least a year away. In which case, we might choose to follow up every three to six months, or so – a process that most scientists seem to value. Until the marketing requirements are fulfilled, the scientist is obliged to fund their idea using their own grants, for example.

Koa Accel does not finance university research. But, as university or hospital technology-transfer groups stand to profit handsomely by licensing technology, we're happy to help them maximize the value of their product.

The overarching goal of Koa Accel is to obsessively mitigate risk, and the greatest risk comes in choosing the right companies to accept in the first place. This is different from a venture capitalist's perspective, because we aren't picking medical device companies; we're picking medical devices. We pass on opportunities that are fabulous device ideas if they don't fit our process.

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Market Intel: After A Year Of Partnerships, Insulin Pump Manufacturers Will Face Fierce Competition In 2020

MARION WEBB marion.webb@informa.com

The combined insulin pumps market is expected to see double-digit growth, reaching more than $5bn by 2023. Dominated by four major players and several innovative start-ups, the insulin pumps market is highly competitive and undergoing significant change. *(Also see "Market Intel: Insulin Pumps Dominate $7bn-Plus Global Infusion Devices Market" - Medtech Insight, 18 May, 2018.)*

While 2019 was marked by collaborations, 2020 will be the year of major product launches and heated competition. Three of the four major players – Medtronic PLC, Insulet Corp. and Tandem Diabetes Care Inc. – are gearing up to introduce their next-generation hybrid closed-loop systems in the US, offering physicians and patients integrated devices to make it easier to collect and interpret data, and manage the disease.

Viral Shah, assistant professor of medicine and pediatrics at the Barbara Davis Center for Diabetes at the University of Colorado in Denver, told *Medtech Insight* the field is changing rapidly, driven not only by technological innovation, but also by the diabetes community, which is putting pressure on regulators to approve products faster and insurance companies to be more flexible.

Shah said he liked the concept of the Tidepool Loop, kicked off by Tidepool, a diabetes data nonprofit that is currently working with the US Food and Drug Administration on an approved version of Loop, a popular do-it-yourself (DIY) open source, automated insulin-delivery system.

Palo Alto, CA-based Tidepool is currently working with Insulet on a future version of the Omnipod system. It is also working with Medtronic on a Bluetooth-enabled MiniMed pump, and with Dexcom Inc. to support its G6 continuous glucose monitoring (CGM) system.

The original Loop was created as part of the #wearenotwaiting movement, giving diabetes patients the tools to develop their own tech-based solutions by "mixing and matching" devices to better manage their condition.

TidePool CEO Howard Look, who has a daughter with type 1 diabetes, told *Healthcare Innovation*: "We believe that people living with diabetes should have a choice, and by creating Tidepool Loop we will be demonstrating the power of an interoperable ecosystem. Some people may prefer a patch pump, others may prefer a tubed pump. Tidepool Loop will also let people with diabetes choose to control their diabetes therapy directly from their iPhone or Apple Watch, which is also a very attractive option for many people."

Shah echoed tthis view: "I really like the concept that it will provide a lot of different options to people and let people take charge, rather than an insurance company giving you a system."

But he foresees challenges as well. "The problem is that I don't know what will happen in real life." Most patients rely on their insurance company to pay for an insulin pump and most insurers only cover one pump every four years; Medicare will pay for one every five years.

"In DIY [insulin delivery], you have options, but then your insurance will limit you to use only one or two devices," he added. He believes that diabetes patients will continue to pressure insurers and regulatory bodies to offer them more choices in managing their diabetes care. This has already begun. "The DIY has a hashtag [wearenotwaiting] – these are the people who forced the regulatory agency to change the approval process."

DEMOGRAPHICS

Diabetes is a major global health challenge. According to 2017 statistics by the International Diabetes Federation, about 425 million adults worldwide between 20-79 years of age have diabetes. By 2045, about 629 million people are expected to be diagnosed with diabetes.

In 2017, more than 1.1 million children worldwide were living with type 1 diabetes, more than 352 million people were at risk of developing type 2 diabetes, and 212 million people with diabetes were undiagnosed. About 4 million people died of the disease.

Global health costs to treat diabetes totaled about $727bn in 2017, or 12% of total health expenditures spent on adults worldwide in 2017. In the US, the total cost to treat diabetes reached about $327bn in 2017.

Automated insulin pump systems, such as Medtronic's MiniMed systems, typically cost $4,000 to $7,000 or more, not including disposables/consumables, which can add thousands of dollars per year, according to a new report by Informa's Meddevicetracker, "Diabetes Management: Insulin Pump Market." And next-generation insulin pumps that feature colorful displays and integrated CGM system sensors, which accurately and continuously measure glucose and relay data to the pump, will add to the overall cost.

INSULIN PUMP MARKET FORECAST

There is still significant room for growth in the global insulin market. Market penetration for pumps is low. San Diego-based Tandem estimates that around 30% of diabetes patients use insulin pumps, which

leaves ample opportunity for companies to take up market share.

According to the Meddevicetracker report, the global market for insulin pumps will grow to $5.1bn in 2023, a compound annual growth rate of about 12.4%, driven by a strong need for improved, automated insulin delivery to lessen the complexity, daily burden and potential health risks that result from multiple daily insulin injections. (See Figure 1 at right.)

Developing systems that help patients achieve better glycemic control remains a major goal of insulin pump manufacturers.

The American Diabetes Association's recommendations for daily "time-in-range" is 70-180 mg/dL for people with type 1 and 2 diabetes. CGMs can help people with diabetes better manage their glucose levels and stay within the target range to avoid glucose highs and lows. Insulin pump makers aim to improve the time-in-range, or time spent in "normal glucose levels," to 80% or more. The goal is to help patients maintain normal glucose levels most of the time.

Shah explained that a CGM, coupled with an insulin pump, offers patients more flexibility because the algorithm in the embedded sensor modulates insulin delivery throughout the day and night, which helps patients stay within set glycemic targets. *(Also see "Market Intel: Needle-Free Glucose Monitoring, Digital Solutions Are Game-Changers In Growing Diabetes-Monitoring Market" - Medtech Insight, 6 Dec, 2018.)*

Medtronic – which was first to gain FDA approval for its MiniMed 670G hybrid closed-loop system in September 2016, with market launch in June 2017 – led the insulin pumps market in 2018 with a 75% market share. This is based on total sales of MiniMed pumps and related supplies, yielding revenues of more than $2.1bn.

Acton, MA-based Insulet ranked second with a 17% global market share and an estimated $496m in sales from its Omnipod line.

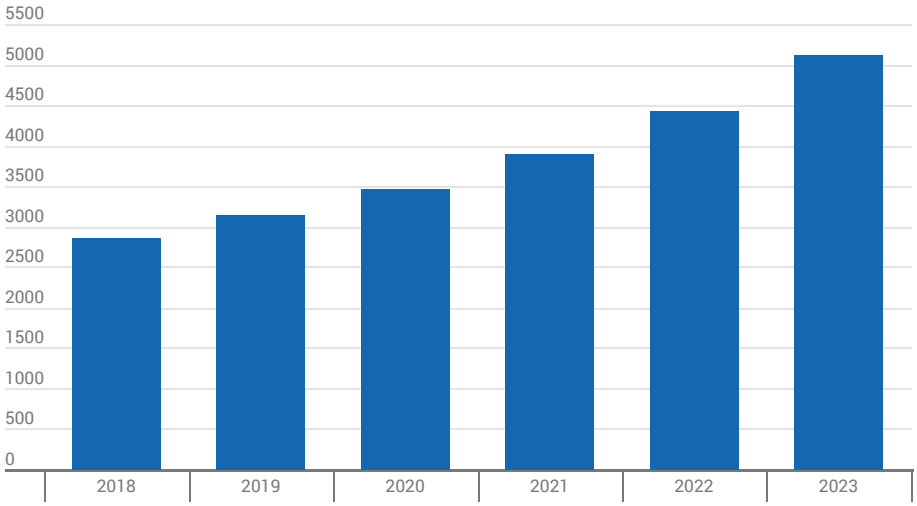
Tandem ranked third, with a 6% market share and $184m in sales. This company, in particular, has made significant inroads re-establishing itself in recent years due to its innovative pump design and technology.

And Bridgewater NJ-based Valeritas Holdings ranked fourth with a 1% market share and $26m in revenues. (See table on p. 18.)

FIGURE 1

Insulin Pumps, Global Market Forecast ($m), 2018-'23

CAGR, 2018-'23, 12.4%



Source: Meddevicetracker, "Diabetes Management: Insulin Pump Market"

MEDTRONIC

Medtronic's lead remains solid due to strong demand for its new sensor-augmented insulin pump portfolio, ongoing launch of the MiniMed 670G in international markets, including in Western Europe and emerging markets, good payer coverage and expanding reimbursement. But the medtech giant is facing rising competition in the US.

Tandem is seen as Medtronic's most significant threat due to the company's user-friendly touchscreen t:slim pump, proprietary algorithms and other technical advancements that set it apart from competitors. Insulet has also created a niche in this market and is experiencing double-digit growth due to strong US sales. And several start-ups, including Bigfoot Biomedical Inc., Beta Bionics Inc., Diabeloop, EOFlow and Ypsomed, which are discussed in the second part of this analysis, are also expected to make in-roads with new product launches in 2020.

During Medtronic's fiscal year 2020 second-quarter conference call on 19 November, CFO Karen Parkhill said: "In diabetes, which represents 8% of our sales, we now expect low single-digit organic growth, reflecting competitive pressures in the US while we await new product approvals."

Parkhill noted that the company was preparing for the launch of its next-generation MiniMed 780G advanced hybrid closed-loop system with Bluetooth connectivity, and expects to announce pivotal data from a study of 350 adult and pediatric type 1 patients at the Advanced Technologies & Treatments for Diabetes conference in Madrid in February 2020.

In February 2019, the FDA granted Medtronic a breakthrough device designation, which is assumed to be the MiniMed 770G or 780G.

The MiniMed 780G's algorithm is expected to be more accurate and is designed to provide automatic correction boluses, which the MiniMed 670G does not provide. Pending FDA approval, the MiniMed 780G system, which is expected to hit the market in 2020, will compete against Tandem's t:slim X2 insulin pump system with its enhanced Control-IQ algorithm, currently under FDA review.

Tandem's t:slim X2 pump system with Basal-IQ technology, a predictive low glucose suspend technology, was FDA-

TABLE 1

Selected Leading Automated Insulin Pumps And Hybrid Closed-Loop Systems

PRODUCT	FEATURES	COMMENTS/STATUS
INSULET CORP.		
Omnipod Insulin Management System	• Tubeless, waterproof, disposable pod/patch pump that attaches to the body • Provides 72 hours of insulin delivery; holds up to 200 units (U-100) of insulin; user fills pod with insulin • Wirelessly communicates with PDM, which programs insulin delivery • Cannula inserts automatically with push of button on PDM	• Insulet claims it is the leading pediatric pump
Omnipod DASH	• Next-generation pump • Free PDM with purchase of pods • Bluetooth wireless connectivity to smartphone-like PDM • Access to new mobile apps • Also used with Contour NEXT One meter	• 510(k)-cleared (June 2018); launched in Q1 2019 • Only pump to receive both DTSec and ISO 27001 certification for cybersecurity • New co-payment plan
Omnipod Horizon Hybrid Closed-Loop System	• Next-generation hybrid closed-loop AP system • Includes personalized/customizable features accounting for variables (diet/exercise, etc.)	• US pivotal trial planned for Q4 2019 • If approved, expected launch in second half of 2020 • Tidepool partnership to develop hybrid closed-loop system for iPhone/Apple Watch
MEDTRONIC		
MiniMed 630G (US)/640G (ex-US)	• SmartGuard "suspend on low" algorithm that can suspend insulin delivery for up to two hours based on CGM reading and preset low • Predictive alerts up to 30 minutes in advance • Built-in Enlite sensor and Guardian sensor (worn up to seven days) • Bolus Wizard calculator helps calculate bolus • Works exclusively with Ascensia's Contour NEXT LINK 2.4 meter	• Automated insulin pump for continuous insulin delivery • While sharing the same platform, it is not technically classified as a hybrid closed-loop system like the 670G (does not include auto mode/"suspend before low" features, as in 670G)
MiniMed 670G	• SmartGuard algorithm • Only system with two modes: auto mode and "suspend before low" • Includes next-generation Guardian Sensor 3 (with seven-day wear and low MARD/high accuracy); however, still requires fingerstick calibration • Works exclusively with Ascensia's Contour NEXT LINK 2.4 meter	• FDA approved (September 2016) • Launched in US (June 2017) • CE mark (June 2018) • First automated, intelligent hybrid closed-loop system, or "artificial pancreas" • First to automatically adjust basal insulin every five minutes based on CGM readings (auto mode) • First to automatically halt insulin delivery 30 minutes before reaching the patient's preset low limit and automatically restart insulin when glucose levels normalize ("suspend before low" mode) • Approximately 180,000 units sold to date • New Flex subscription plan ($50/month)
MiniMed 770G	• Next-generation interoperable AP system using Tidepool's open-source algorithm (Tidepool Loop app) • An automated hybrid closed-loop insulin delivery app for the iPhone and Apple Watch • Wireless/Bluetooth connectivity	• Under development
MiniMed 780G	• Next-generation 670G with an improved algorithm • Will automate correction boluses (to compete with Tandem's Control-IQ) • New, improved Guardian CGM will lower required fingerstick calibrations to first day only • Goal of increasing time-in-range to 80% or more, a significant breakthrough • Wireless/Bluetooth connectivity	• Undergoing clinical trials • Expected CE mark and launch by end of 2020

PRODUCT	FEATURES	COMMENTS/STATUS
ROCHE		
Accu-Chek Solo micropump	• New, small, lightweight semi-disposable, tubeless micropump • Operates using a fully featured remote control • Includes built-in blood glucose monitoring and bolus control	• CE mark (October 2018); only available in Europe in selected markets
TANDEM DIABETES CARE		
t:slim X2 with Basal-IQ	• Automated touchscreen pump • Smaller than competitor devices • Wireless/Bluetooth connectivity • Predicts 30 minutes in advance and adjusts insulin automatically • Holds up to 300 units of insulin • Works with new Dexcom G6 (no fingersticks and 10-day wear) • Compatible with iCGM devices • Option to use with or without the Basal-IQ feature and CGM	• FDA approved (June 2018) • CE mark (April 2018) • Only automated pump approved in children as young as 6 • Only iCGM pump allowing integration with any CGM
t:slim X2 with Control-IQ	• Next-generation hybrid closed-loop AP system, improves upon Basal-IQ algorithm • Touchscreen • New automatic/autocorrect bolus feature to automatically adjust for high blood glucose • New interoperability • Dexcom G6 sensor (10-day wear/no fingerstick calibration)	• Expected launch in US in Q4 2019 • International launch in 2020
t:sport	• Automated insulin pump with next-generation algorithm • Half the size of the t:slim X2 • Uses a 200-unit insulin cartridge and short infusion set • Controlled using a mobile app or remote handheld device	• Under development
t:connect	• Will allow remote control using a cell phone • Wireless software updates • Personalized health app with diet, sleep, and exercise data, and decision support • Biometric authentication security	• Under development
VALERITAS HOLDINGS INC.		
V-Go	• Daily disposable patch-based insulin-delivery device; must be removed and refilled with insulin daily • Weighs approximately 1 oz. • Worn discreetly under clothing • No electronics, batteries or infusion sets • Available in a preset basal rate that delivers 20, 30 or 40 units of insulin daily	• 510(k)-cleared (2010) and CE mark (2011) • Indicated for type 2 diabetes (not type 1)

Source: Meddevicetracker, "Diabetes Management: Insulin Pump Market"

approved in June 2018 and CE-marked in April 2018. The FDA later also granted Tandem the ability to market its t:slim X2 pump as an interoperable pump, also known as an alternative-controller-enabled pump, a designation that allows integration with other externally produced components, a significant selling point over rivals that don't have integrated glucose monitors.

The t:slim X2 is the first and only automated insulin pump approved for children 6 and older. It works with Dexcom Inc.'s G6 CGM, so it does not require fingersticks for mealtime dosing or calibration, and does not emit excessive alerts or alarms, a major concern raised by MiniMed 670G users. It is smaller and more discrete than previous pumps and can hold up to 300 units of insulin.

Shah also believes that Tandem's t:slim X2 will be able to compete with Medtronic in terms of rapidly doing clinical studies and continued innovation, pointing to current device limitations with Medtronic's 670G, which include "bothersome alarms and alerts, exits from auto mode, sensor failures and manual calibration requirements."

"Most patients are frustrated about the sensor in the 670G – they still have to cali-

brate about three to four times a day, and there are unnecessary alarms and alerts that the patients are annoyed about," Shah said. He said that 30% of type 1 diabetes patients on insulin pumps at the Barbara Davis Center have stopped using the 670G due to dissatisfaction with the way it provided glucose control. The company also recently announced safety concerns with its MiniMed 600 series. *(Also see "Medtronic Warns On Insulin Pump Safety" - Medtech Insight, 27 Nov, 2019.)*

Shah said given that most insurers only pay for an insulin pump every four years, patients will continue using the Medtronic insulin pump, but opt for a different CGMs, with Dexcom's being the preferred CGM.

Medtronic's next-generation Guardian CGM sensor, which is in development, will reduce fingerstick calibration by about 95%, and the company is eyeing the coveted "nonadjunctive" labeling claim, which allows CGMs to be used for insulin dosing in lieu of a fingerstick glucometer. Dexcom, Abbott Laboratories Inc. and Senseonics Holdings Inc. have all received that indication. *(Also see "Market Intel: CGM Market Competition And Device Interoperability Were Hot Topics At ADA2019" - Medtech Insight, 3 Jul, 2019.)*

Medtronic's $2.4bn diabetes group portfolio, however, remains a force to be reckoned with.

Medtronic has significantly more financial resources than its competitors and established relationships with health-care professionals, customers and third-party payers. It also has a larger R&D budget and pipeline than its competitors, Meddevicetracker noted.

The company also benefits from "transitioning patients" from former major rivals Animas Corp. and Roche, which announced their exit from the US insulin pump market in 2016 and 2017, respectively.

Medtronic is serving the insulin supply needs of Animas and Roche patients. Insulet and Tandem are also benefiting from transition patients, but to a lesser extent.

That said, Roche has not exited the insulin pump market outside the US. It has developed the new Accu-Check Solo micropump system, which received a CE mark in 2018 and is currently sold in Europe.

TANDEM

Tandem has seen stellar revenue growth over the past year, including outstanding third-quarter earnings. The company had $95m in worldwide sales during the third quarter of 2019, marking the "third quarter in a row with greater than 100% sales growth year-over-year," Tandem CFO Leigh Vosseller said during a 4 November third-quarter earnings call. The company's global insulin pump shipments exceeded 17,800 in the first quarter, up from 8,434 during the same quarter in 2018. Tandem estimated its 2019 sales to be in the range of $358m to $365m, including international sales of $58m to $60m.

Kim Blickenstaff, Tandem's former CEO and current executive chairman, told investors during the call that "excitement is high around Tandem as well as across the diabetes community for our Control-IQ approval," and that there were no "concerning issues" with the FDA.

He also told investors that he expected findings from the Protocol 3 study (DCLP3) of the National Institutes of Health-funded International Diabetes Closed Loop (iDCL) trial using the t:slim X2 pump with Control-IQ technology to be "invaluable in our conversations with clinicians as well as payers following FDA approval." The results were published in the *New England Journal of Medicine* in October.

John Sheridan, Tandem's president and CEO, told investors: "I think we expect that we'll have the same sort of momentum in 2020 that was in 2019. We will be competing against Medtronic's new product, which I think is intended to be introduced in the mid-year timeframe. We'll have momentum already built up on Control-IQ by that point in time. And the ease of use and simplicity of our device is going to continue to differentiate us when you do compare us with those devices."

The Control-IQ launch will be concurrent with the launch of Tandem's new mobile app, which will allow patients to wirelessly upload data from their pump in CGM to their t:connect management app.

"This is a significant feature, as it takes away a manual step for our customers and their health-care providers of having to upload pumps through USB in order to track and see trending information," Sheridan said.

Tandem plans to quickly expand the reach of Control-IQ to the pediatric market and file for FDA approval for use in children 6 and older. The company is also developing a modified wearable version of the its flagship pump. The t:sport is roughly half the size of the t:slim X2, and is targeted for a 510(k) submission for the summer of 2020.

INSULET

Insulet CEO Shacey Petrovic told investors during a 5 November third-quarter earnings call that the company had another period of "record patient starts on its pump therapy." The company reported third-quarter revenues of $192.1m, up 27% compared with $151.1m during the same quarter a year earlier.

The Omnipod is a wireless Bluetooth system that connects to a touchscreen, handheld personal diabetes manager (PDM) with a waterproof, tubeless continuous insulin delivery "pod," or pump. The PDM, which controls insulin delivery, looks like a smartphone and is available with two new apps that help users manage and share diabetes data and accessories.

In September, the company announced it had received FDA clearance to market its Omipod DASH insulin management system as an integrated insulin pump, allowing it to be part of an interoperable automated insulin delivery system, such as the company's Omnipod Horizon hybrid closed-loop system, which is in development. *(Also see "Insulet Wins FDA Clearance For Omnipod ACE Pump" - Medtech Insight, 23 Sep, 2019.)*

Petrovic said the Horizon system, in development with Tidepool, will be studied in a pivotal trial in December, with targeted marketing launch in the second half of 2020.

The company has made significant progress this year. It broadened the Omnipod DASH coverage for commercial, Medicare and Medicaid beneficiaries. Petrovic told investors that Medicare beneficiaries "continue to represent a growing percentage of our Omnipod users."

The company has also benefitted from increased adoption by type 2 patients, thanks to increased sales through phar-

macy channels. The company adopted a new payment model, where patients do not pay upfront for the Omnipod DASH. Instead, they pay only a co-pay of $35 or less, typically every three months, after obtaining a pod at the pharmacy, Insulet's CCO Bret Christensen told *Medtech Insight* at the American Diabetes Association's annual meeting. *(Also see "Device Week, July 6, 2018 – Clinical Data Presentations At ADA; Big Deals From GE, Novartis And BioTechne" - Medtech Insight, 6 Jul, 2018.)*

The company raised its revenue guidance for 2019 to $722m to $730m, representing growth of 28% to 29%, up from 24% to 27% previously.

VALERITAS

Valeritas, which markets the V-Go, a small, wearable insulin delivery system designed specifically for type 2 diabetes patients, also recently announced positive third-quarter earnings.

For the third quarter, Valeritas posted revenues of $8.5m, a 20% increase over the same quarter in 2018, with total prescriptions in the US growing more than 25%.

The company also announced positive data in October from a retrospective study comparing V-Go patients with patients using multiple daily injection (MDI) therapy. The results showed that during the last six months of therapy, V-Go users decreased their daily insulin dose by 29 units a day compared with the MDI group, which increased their daily insulin dose by 6 units a day.

The V-Go group saved about $1,300 in total diabetes medication costs, compared with the MDI group. The results are published in the *Journal of Managed Care & Specialty Pharmacy*.

The V-Go is currently cleared by the FDA to deliver U-100 rapid-acting insulins, such as Humalog and novolog, but Valeritas filed for a 510(k) modification with the FDA to use the less-costly regular insulin. The modification is based on a study that showed type 2 patients that used the less costly U-100 regular human insulin had similar A1C or glucose levels to type 2 patients who used V-Go with fast-acting U-100 insulin.

"We believe this data are profound, as the use of regular human insulin could save US patients with type 2 diabetes in health-care systems thousands of dollars per year, and could lead to better patient compliance, resulting in potentially improved blood glucose because they're actually using the product in delivering insulin," Valeritas president and CEO John Timberlake told investors in a 19 November earnings call. The company is also hoping to bring a Bluetooth-connected accessory device to market. The V-Go SIM is an accessory that will snap onto the V-Go. It detects and records basal and bolus insulin usage, and wirelessly sends that information to the SIM smartphone app.

On the subject of diabetes costs, Shah noted that in Colorado this year, legislation was passed that will cap total monthly insurance co-pays for insulin at $100, forcing all insurers in the state to comply with the new regulation by 1 January 2020. The passage of the law was supported by the American Diabetes Association.

Other states are also considering reducing the economic burden of insulin pricing, a measure that Shah applauds.

"I think that many states will follow Colorado['s example] – buying regular insulin from a pharmacy would cost you about $40 to $50 per vial, and if you need two vials in a month you would be paying $100. So, if you can get a rapid-acting human analog at $100, why would you pay $100 for regular insulin?" Shah said.

Shah said he's excited about the future.

"I think the next few years will be every interesting. I have no doubt [many new developments in the field of diabetes] will definitely benefit patients."

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sectors subtables at https://bit.ly/2PbPhmY, but also extend to dental, ophthalmic, wound care, diabetes and, in the example of Grifols SA, plasma collection and blood diagnostics. In 2018, Spain's largest medtech player consolidated its Top 20 ranking by, among other things, completing the acquisition of Biotest Pharmaceuticals Corp. Grifols had divisional IVD sales of $829m in 2018, and thus remained outside the IVD Top 10.

The only UK company among the leading 25 medtechs, Smith & Nephew PLC, recently parted company with CEO Namal Nawana after 18 months in the job. He was on a mission to sharpen S&N's focus and embark on more M&A, but left over remuneration issues. Now in charge is Roland Diggelmann, a former Roche Diagnostics Corp. executive, who must decide whether to accelerate Nawana's policy of deal-making as a way of growing S&N's ortho recon, sports medicine and wound-care businesses. The UK company has lost ground over the years in the ortho segment to other, more adventurous rivals. In spring 2019, reported talks with spinal company NuVasive Inc. came to nothing. It did complete a smaller M&A transaction, the purchase of Osiris Therapeutics Inc. The UK's largest medtech group sits at No. 21 on the Top 100 list, as it did in 2017, with below-average 2018 sales growth of under 3%. NuVasive, meanwhile - less than a third the size of S&N's ortho franchise - put on industry average growth of 6.8% in 2018.

THE GLOBAL TOP 10: A CURATE'S EGG

Within the Top 10 companies, all of which were comfortably in the double-digit, billions-of-dollars-ranked sales, Becton Dickinson & Co. was the standout riser in 2018. It added almost a third to its 2017 sales in rising three places to No. 7, with 2018 sales knocking on the door of $16bn (including IVD sales, which were up 8.6%). The reason was the $24bn acquisition of Bard, with which BD claims a "unique position in both treatment of disease and processes of care for providers." Clinician satisfaction in terms of device usage and ease of handling has become a much higher-profile USP for many medtech manufacturers in recent years.

BD will hope that incoming CEO and president Thomas Polen, an internal appointment, will emulate the record of growth under Vincent Forlenza, who retires as chairman and CEO on 28 January 2020. Recent track records would suggest so: under Forlenza, Polen led the acquisitions of both Bard and, in 2015, CareFusion Corp., which lifted BD into the big leagues.

This pace of growth saw BD rise above Cardinal Health Inc., but still remain $3bn behind fifth-placed Abbott Laboratories Inc., which has also been tearing up the tarmac in M&A in past years. Its 2017 consolidation of St. Jude Medical Inc. has made it the second-leading cardiovascular group. In 2018, it fully consolidated the October 2017 purchase of diagnostic device and service provider Alere Inc., establishing itself as a leader in point-of-care testing (POCT), and gaining access to new channels and geographies. Overall, it was the second-highest sales climber in the Top 10 in 2018, up by almost 17%. And with its bulked up IVD business – its IVD sales rising by 33% in 2018 – Abbott is now also clearly the second-largest global IVD group by sales. In that industry segment, it sits behind pureplay Roche, whose $13.2bn IVD revenues in 2018 kept it as a top 10 global medtech group.

Fellow European diagnostics player Siemens Healthineers AG made IVD sales of €4.13bn, a rise of 4.3% in the year ended 30 September 2019, and remained the fourth-largest global IVD group behind Danaher Corp., which came in third. Siemens Healthineers' strong imaging (€8.94bn) and advanced therapy (€1.6bn) revenues helped elevate the German group to sixth-largest medtech group in the current Top 100.

The weakest growth among the Top 10 came at Cardinal Health, whose merely marginal increase illustrated the "curate's egg" nature of performances in the Top 10. Here, it was a case of timing: in fiscal year 2018 (2017-'18), Cardinal's medical segment revenue grew powerfully, with $1.9bn of revenues coming from new acquisitions, primarily the patient-recovery business. That cannot be repeated every year, especially once divestitures – in 2018, it sold its China distribution and the naviHealth businesses – are factored in.

BELOW-AVERAGE GROWTH FOR MANY LEADING COMPANIES

The rest of the Top 10 saw average or below-industry-average growth in 2018: Stryker Corp., under 5%; GE Healthcare 4%; and Philips Healthcare, 2.4%. And that also goes for the global leaders Johnson & Johnson, No. 2 in the ranking, and Medtronic, No. 1. J&J's slim 1.5% medtech segment sales rise in 2018 followed its sale of Codman Neuro to Integra LifeSciences Holdings Corp. (which increased its sales by 24% and added incremental revenue of $236m). That, plus a loss of spinal-market share, led to a 1.9% dip in J&J's orthopedic sales. Its diabetes sales also dropped by 37.5% to $1bn as a result of the divestiture of its LifeScan Inc. business in Q4 2018, and the Q4 2017 decision to exit the Animas Corp. insulin pump business.

In diabetes, the reverse was the case at global medtech leader Medtronic PLC, which, as signaled last year, became the first global $30bn dollar medtech group – albeit on the strength of a lowly 2% sales rise. Its diabetes business (insulin pumps, CGM, insulin-pump consumables and therapy management) led the growth, at 12%, recording a business group total of $2.4bn. Year-end April 2019 growth was assisted by demand for the MiniMed 670G hybrid closed-loop system with SmartGuard technology (which mimics some functions of a healthy pancreas and maximizes time in range). Its Guardian Connect CGM system was a brand in high demand.

Next year, Medtronic will be setting group strategy without the deft touch of long-serving CEO Omar Ishrak, whose retirement at the close of the 2020 fiscal year will make way for internal appointee Geoff Martha. The big strategic news for Medtronic in 2018 was its acquisition of robotic guidance systems company Mazor Robotics Ltd. for $1.6bn. In 2019, it continued to build its robotics reach.

ACTIVITY OUTSIDE THE TOP 10

All eyes have been on Boston Scientific Corp.'s drive to expand organically and externally. In 2018, besides spending an impressive 10% on R&D (as much as high-tech companies), it made seven acquisitions, and did VC investments in another 30-40 companies, including options to buy. One of these was the biggest M&A bid of 2018, the $4.24bn acquisition of vascular and oncology device maker BTG PLC. The deal was completed later than initially anticipated, in August 2019. Boston must sell BTG's embolic microspheres portfolio to Varian Medical Systems Inc., and will only feel the full consolidated benefit of BTG in 2020. In 2018-2019, BTG recorded 12-month MAT medtech sales of $365m, keeping its name within the Top 100 (at No. 85) for one last year.

Boston's policies are all aimed at category leadership, achieved largely by adding adjacencies. Its 2018 M&A activity extended to the addition of nVision Medical Corp. (platform for potential earlier diagnosis of ovarian cancer); Augmenix Inc. (technology to reduce side-effects of prostate cancer radiotherapy); NxThera Inc. (a minimally invasive treatment for BPH); Claret Medical Inc. (TAVR safety technology); and Cryterion Medical Inc., an electrophysiology business, with which Boston can offer both cryothermal and radiofrequency single-shot, balloon-based ablation therapies.

Even without BTG, Boston recorded above-average sales growth of 8.6% in 2018, and can expect to become the 11th global double-digit million sales medtech group once 2019 audited results are released.

There was little to catch the eye in the placings immediately below Boston, with low-to-average growth reported by Danaher (+5.3%), and Alcon Inc. (+5.6%), while Zimmer Biomet Holdings Inc.'s second-half 2018 uptick could not lift sales growth for the year above a lowly 2%.

93% OF LEADING COMPANIES IN GROWTH

As per the usual form among the flagship companies of the publicly traded medtech industry, very few of the billion-dollar sales groups saw reduced revenues in 2018. Agfa Corp. was "flat" following reorganization of distribution channels in China. *Medtech Insight* has been unable to establish the reasons for Japanese IVD company Miraca Holdings Inc. going backward in both yen and US dollar-converted sales in 2018; or for China's Shinva Medical Instrument's slippage in US dollar sales. Further down the listing, Japan's Konica Minolta Inc., Swiss drug-delivery company Ypsomed,

Stratec Biomedical and Endologix Inc. saw lower sales for different reasons in 2018. Konica Minolta's health-care business sales dip was blamed on the discontinuation of sales of certain purchased products. In Stratec's case, it was due to launch postponements, and lower sales volumes from established systems, parts, consumables and services. Endologix has been restructuring its US and European sales teams and coping with field safety notices (for its AFX System and Ovation System), and lower sales of the Nellix endovascular aneurism sealing system. Ypsomed said its sales would have been up by 24% if its 2018 dispute with Insulet Corp. over the mylife OmniPod distribution agreement, leading to arbitration proceedings, been excluded from consideration. Even so, 93% of the Top 100 reported sales growth in 2018.

TRADING PLACES

While at the top of the industry, Medtronic recorded sales upwards of $30bn, the threshold for Top 100 status in our listing of publicly held, reporting companies has dropped again, by some $40m, reflecting the ongoing consolidation of the industry. Refractive surgery implantable lens maker Staar Surgical Co. is newly admitted to the Top 100 on the strength of a 2018 sales rise of 36%, despite competition from laser vision surgery, where Novartis AG (Alcon), J&J (AMO), Bausch Health Companies Inc. and Carl Zeiss Meditec AG have major strengths. Bespak Europe Ltd.'s drug-delivery technologies recorded a small rise in US dollar sales, and franchise owner Consort Medical PLC (UK) was elevated to Top 100 status in 2018, as was Swedish imaging IT and digital pathology company Sectra AB, on the back of a 17% rise in 2018-'19 local currency sales. Recipharm AB agreed in November 2019 to acquire Consort Medical.

Making way for these new entrants, besides Bard and Alere, was Analogic Corp., which in 2017 was a $475m revenue group, and remains active in ultrasound, advanced imaging and real-time guidance technologies. In 2018, it was acquired by an affiliate of Altaris Capital Partners, and, now privately held, has been delisted from NASDAQ and is no longer eligible for inclusion in our top 100 list.

In 2020, besides BTG, the US orthopedic and sports medicine group DJO Global Inc. will also be a name – if not brand – consigned to league table history. The $1.2bn revenue group was acquired by Colfax Corp for $3.15bn in November 2018 (completed February 2019). DJO will help make Colfax a higher-margin, faster-growing and less cyclical company, says Colfax, which plans to bring DJO within its "CBS" culture – a business management system that uses repeatable, teachable processes to "drive continuous improvement and create superior value for customers, shareholders and associates."

Longer term, Colfax envisions DJO as the foundation of a new growth platform in the $21bn high-margin orthopedic solutions market. In DJO, it sees a business that is well positioned to benefit from "secular trends that are being driven by changing demographics and increased preventive health care." Exploiting these trends is seen by the broader industry as a key way of anticipating and meeting changing health-care demands in the future, and remaining competitive.

DEXCOM SHINES AMONG MIDDLE-GROUND PERFORMERS

Net of companies exiting by way of consolidation, the medtech industry and the Top 100 list gained two more dollar billionaire revenue earners in 2018, both from internal growth: Japan-based blood pressure monitor maker Omron Corp. and diabetes monitoring company Dexcom Inc. Companies over this sales threshold make up 60% of the Top 100.

CGM device manufacturer Dexcom's sales leapt by more than 43% in exceeding $1bn 2018. Its gains, made exclusively organically, were driven primarily by increased volumes of disposable sensors and durable systems. The company's G4, G5 and G6 systems compete directly with technologies from Medtronic, Roche, LifeScan, Abbott and Ascensia Diabetes Care (which has annual sales at or around €1bn). Senseonics and Medtrum are also in the CGM mix.

The seven largest US private third-party payers have all issued coverage policies for CGMs. But while Dexcom's sales are booming, at the other end of its P&L, it continued to report operating losses ($186m in 2018) – as it has done since its inception in 1999.

FAST-RISER CLUB

Other eyecatchers in the lower rankings include human tissues supplier CryoLife Inc., whose 39% rise in sales included a full year of revenues from Jotec, a German endovascular and surgical products company. However, the bottom line was a net loss of $2.8m, due largely to the financing needs to integrate that very acquisition.

MicroPort Scientific Corp. revenues in 2018 were also acquisition-enhanced, growing by 49% (32%, excluding the impact of foreign exchange). Expanded sales on the global market and an improved orthopedics portfolio were augmented by the positive effects of the acquisition of LivaNova PLC's CRM business.

On the contrary, Cardiovascular Biosystems' 14% sales rise (peripheral and coronary products) originated in increased customer accounts, growth in hospital and office-based lab sites, international expansion, and additional product offerings – and all against what it said were modest average selling price declines.

But the blue ribbon for 2018 sales growth should go to IVD company Quidel Corp., whose 2018 revenues increased by 88% to well over half a billion dollars, due primarily to the acquisition of the triage and BNP businesses from Alere in fall 2017. The acquired business represented 51% of Quidel's 2018 revenues.

Colorectal cancer diagnostics company Exact Sciences Corp., not in the 2018 listing based on a large element of its sales coming from performing tests, merits a mention in this context. In 2014, the Cologuard test maker posted sales on $1.8m. In 2018, that had risen to $454.4m, an impressive 71% increase from the previous year, due to more tests being carried out and increased commercial insurance coverage for Cologuard. The company launched a partnership with Pfizer Inc. in 2018. In fall 2019, the test was expanded by the US Food and Drug Administration for use n people over 45 years of age.

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